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LETTER

Spontaneous remission of sexually transmitted diseases must be considered in randomised controlled trials

Randomised controlled trials that test biomedical interventions to reduce sexually transmitted infections (STIs) have had very mixed results,^{1–2} as have behavioural trials.^{3–4} It is only in the past 10 years that the field has recognised that chlamydia resolves itself without treatment in 50% of the cases,⁴ although the estimates range from 13% to 60%.^{5–7} The length of time to clear chlamydia infection varies from 60 days in women to up to 15 months in men.⁵ The speed of resolution is also subject to individual-level factors (eg, infection clears sooner in older people), making it difficult to determine sample sizes for randomised controlled trials with STI outcomes.

In a recent five-country trial,¹ the determination of sample size to identify the necessary number of participants to demonstrate a reduction in bacterial STI was based primarily on chlamydia (65.8% of the bacterial infections observed at recruitment; 10.3% prevalence) and trichomoniasis among women (17.2% of infections; 4.89% prevalence). When we examined all the bacterial STIs 1 year later, the rates of chlamydia were more than 60% lower and the rates of trichomoniasis were 40% lower. Potentially, half of the new chlamydia and trichomoniasis infections may have spontaneously resolved, as suggested by the above studies, but the actual incidence rates may have been 25% more than those observed at 12 months

(assuming a consistent rate of infection over time).

The emerging data on spontaneous remission rates raises serious questions on how to design effective evaluations to demonstrate reductions in STIs. Randomised controlled trials must be designed to have shorter periods between assessments. It is also likely that there is a variance in the rates of clearance, although it is unclear in what direction and for whom the variations will apply. Thus, the design of future multisite trials must *cautiously* estimate STI infections, given the emerging data on spontaneous remissions or clearing of infections, and consider much shorter follow-up periods, even for long-term longitudinal trials.

Mary Jane Rotheram-Borus,¹ Zunyou Wu,² Li Li,¹ Roger Detels,¹ Li-Jung Liang,¹ and the NIMH Collaborative HIV/STD Prevention Trial Group

¹University of California at Los Angeles, Semel Institute for Neuroscience and Human Behavior, Center for Community Health, Los Angeles, California, USA;

²National Center for AIDS/STD Control and Prevention, Chinese Centers for Disease Control and Prevention, Beijing, China

Correspondence to Dr Mary Jane Rotheram-Borus, University of California, Semel Institute for Neuroscience and Human Behavior, 10920 Wilshire Boulevard, Suite 350, Los Angeles, CA 90024, USA; cchpublications@mednet.ucla.edu

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